

IN THE CLAIMS:

Please cancel claims 1-73, 75, 80, and 82-87 (as indicated below) without prejudice to further prosecution in one or more related continuation or divisional applications. Please amend claims 74 and 81, and add new claims 88-103 as follows:

1-73 (Canceled).

74. (Currently Amended) A nucleotide incorporating enzyme variant that incorporates a non-natural or rare nucleotide analogue at least about 10% as efficiently as a naturally occurring nucleotide,

wherein the nucleotide incorporating enzyme variant is produced by the a method of claim 1, 47 or 60 comprising:

(a) providing a plurality of nucleic acid segments, which nucleic acid segments encode all or part of one or more parental nucleotide incorporating enzymes;

(b) identifying at least one non-natural or rare nucleotide analogue to be incorporated by the nucleotide incorporating enzyme, which non-natural or rare nucleotide analogue is incorporated by at least one of the one or more parental nucleotide incorporating enzymes at an efficiency of less than about 10% the efficiency of a naturally occurring nucleotide;

(c) diversifying the plurality of nucleic acid segments, thereby producing a library of nucleic acids encoding nucleotide incorporating enzyme variants; and

(d) identifying at least one nucleotide incorporating enzyme variant that incorporates the non-natural or rare nucleotide analogue at least about 10% as efficiently as a naturally occurring nucleotide.

75. (Canceled)

76. (Original) The nucleotide incorporating enzyme variant of claim 74, which nucleotide incorporating enzyme variant incorporates the non-natural or rare nucleotide analogue at least about 10 fold more efficiently than at least one of the one or more parental nucleotide incorporating enzymes.

77. (Original) The nucleotide incorporating enzyme variant of claim 74, which variant incorporates nucleotides or nucleotide analogues with low fidelity.

78. (Original) The nucleotide incorporating enzyme variant of claim 74, which variant incorporates nucleotides or nucleotide analogues with high fidelity.

79. (Original) A kit comprising the nucleotide incorporating enzyme variant of claim 74, and one or more of a container, a packaging material, and a natural nucleotide or non-natural or rare nucleotide analogue.

80. (Canceled)

81. (Currently Amended) A kit comprising the nucleotide incorporating enzyme variant of claim 75 76, and one or more of a container, a packaging material, and a non-natural or rare nucleotide analogue, ~~which non natural or rare nucleotide analogue is incorporated by a parental nucleotide incorporating enzyme at an efficiency of less than 10% the efficiency of a naturally occurring nucleotide, and which non natural or rare nucleotide analogue is incorporated by the nucleotide incorporating enzyme variant at least 10 fold more efficiently than it is incorporated by at least one of the one or more parental nucleotide incorporating enzymes.~~

82-87 (Canceled)

88. (New) The nucleotide incorporating enzyme variant of claim 74, wherein the nucleotide incorporating enzyme variant comprises sequence segments from two or more members of a family of nucleotide incorporating enzymes.

89. (New) The nucleotide incorporating enzyme variant of claim 88, wherein the two or more members are naturally occurring.

90. (New) The nucleotide incorporating enzyme variant of claim 74, wherein the step of diversifying the plurality of nucleic acid segments comprises recombining the plurality of nucleic acid segments.

91. (New) The nucleotide incorporating enzyme variant of claim 74, wherein the step of diversifying the plurality of nucleic acid segments comprises recursively recombining the plurality of nucleic acid segments.

92. (New) The nucleotide incorporating enzyme variant of claim 90, wherein recombining the plurality of nucleic acid segments comprises assembling synthetic oligonucleotides.

93. (New) The nucleotide incorporating enzyme variant of claim 92, wherein the synthetic oligonucleotides are joined using only a ligase.

94. (New) The nucleotide incorporating enzyme variant of claim 91, wherein recursively recombining the plurality of nucleic acid segments comprises assembling synthetic oligonucleotides.

95. (New) The nucleotide incorporating enzyme variant of claim 94, wherein the synthetic oligonucleotides are joined using only a ligase.

96. (New) A nucleotide incorporating enzyme variant that polymerizes a polynucleotide in a template dependent manner in the presence of a biological impurity found in blood, plasma, or urine,

wherein the nucleotide incorporating enzyme variant comprises sequence segments from two or more members of a family of nucleotide incorporating enzymes, and

wherein the nucleotide incorporating enzyme variant is produced by a method comprising:

(a) providing a plurality of nucleic acid segments, which nucleic acid segments encode all or part of one or more parental nucleotide incorporating enzymes;

(b) diversifying the plurality of nucleic acid segments, thereby producing a library of nucleic acids encoding nucleotide incorporating enzyme variants; and

(c) identifying at least one nucleotide incorporating enzyme variant that efficiently polymerizes a polynucleotide in a template dependent manner in the presence of a biological impurity found in blood, plasma, or urine.

97. (New) The nucleotide incorporating enzyme variant of claim 96, wherein the step of diversifying the plurality of nucleic acid segments comprises recombining the plurality of nucleic acid segments.

98. (New) The nucleotide incorporating enzyme variant of claim 96, wherein the step of diversifying the plurality of nucleic acid segments comprises recursively recombining the plurality of nucleic acid segments.

99. (New) The nucleotide incorporating enzyme variant of claim 97, wherein recombining the plurality of nucleic acid segments comprises assembling synthetic oligonucleotides.

100. (New) The nucleotide incorporating enzyme variant of claim 99, wherein the synthetic oligonucleotides are joined using only a ligase.

101. (New) The nucleotide incorporating enzyme variant of claim 91, wherein recursively recombining the plurality of nucleic acid segments comprises assembling synthetic oligonucleotides.

102. (New) The nucleotide incorporating enzyme variant of claim 101, wherein the synthetic oligonucleotides are joined using only a ligase.

103. (New) A kit comprising the nucleotide incorporating enzyme variant of claim 96, and one or more of a container, a packaging material, and a natural nucleotide or non-natural or rare nucleotide analogue.